## COOLING APPARATUS FOR A MULTIPLEXED CAPILLARY ELECTROPHORESIS SYSTEM

### Cross-Reference to Related Application

This application is a continuation-in-part of U.S.
5  Application Ser. No. 09/621,890, filed July 20, 2000, by
Peijun Cong and Robert Doolen, titled "Multiplexed Capillary
Electrophoresis System for Chiral Separation", which is
incorporated by reference herein for all purposes.

### Background of the Invention

10        This invention is generally in the field of capillary
electrophoresis, and relates particularly to apparatus and
method for cooling the capillaries of a multiplexed or
"parallel" capillary electrophoresis system.

Capillary electrophoresis (CE) is a chemical separation
15  technique involving the use of one or more capillary tubes.
Parallel CE, a recently developed technique using many
parallel capillary tubes, is growing in popularity since
this technology allows multiple samples to be analyzed
quickly and efficiently.  This is particularly advantageous
20  in combinatorial chemistry where many hundreds and even
thousands of samples are analyzed over a short period of
time.  Parallel CE involves the use of a "bundle" of
capillary tubes, e.g., 24, 48, 96 or other number of such
tubes.  A chemical sample to be analyzed is loaded in each
25  tube, and a high voltage is applied to the tube, causing the
components of the sample to migrate in the tube at different
speeds, thereby causing separation of the components which
can then be analyzed by conventional light absorption or
other techniques.   Reference may be made to the following
30  patents and publications for a more detailed description of
CE, including parallel CE, and various analytical techniques
used in CE:  U.S. Patent Nos. 5,900,934, 5,324,401,
5,312,535,  5,303,021, 5,239,360; C.Culbertson et al.,
*Analytical Chemistry*, 70, 2629-2638  (1998); and X. Gong et
35  al., *Analytical Chemistry*, 71, 4989-4996 (1999).  None of

these publications disclose the use of parallel CE to achieve chiral separation.

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The electrical current passing through the parallel capillary tubes of a CE system can generate a substantial amount of heat, particularly where high voltages and electrical currents are used to achieve the separation of the samples, as during a chiral separation process using chiral buffers, or when CE is run in a micellar electrokinetic chromatography (MEKC) mode where the current

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is high and the temperature rise in the capillary tubes due to Joule heating can be large. If not dissipated, this heat can cause the formation of bubbles in the samples, sparking, and other undesirable results having an adverse affect on separation and analysis. Therefore, there is a need for a

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system for effectively cooling such tubes.

Summary of the Invention

Among the several objects of this invention may be noted the provision of cooling apparatus and a related method useful for preventing overheating of the capillary

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tubes and contents thereof when CE is run in a mode (e.g., an MEKC mode) generating substantial heat; the provision of such apparatus and method having no adverse affect on the separation and/or analytical process; the provision of such cooling apparatus which is adjustable to various cooling

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temperatures; the provision of such cooling apparatus which can be configured to remove a desired amount of heat; the provision of such apparatus which is safe to use.

In general, this invention is directed to apparatus for cooling a bundle of capillary tubes to prevent overheating

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of the tubes during a parallel capillary electrophoresis procedure. The apparatus comprises a jacket of thermally conductive solid material comprising mating jacket members movable between an open position in which the jacket members are separated to allow placement of the bundle in the jacket

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and a closed position in which the jacket members are mated together and the bundle is disposed inside the jacket in

thermally conductive relation with the jacket.  Window
openings in the mating jacket members define a window to
permit the passage of light through the window and the
capillary tubes of the bundle at the location of the window.

5      The present invention is also directed to cooling
comprising  inner and outer jackets.  The inner jacket is of
thermally conductive, electrically insulating solid material
comprising mating inner jacket members movable between an
open position in which the jacket members are separated to
10   allow placement of the bundle in the jacket and a closed
position in which the jacket members are mated together and
the bundle is disposed inside the inner jacket in thermally
conductive relation with the jacket.  The outer jacket is of
thermally conductive solid material comprising mating outer
15   jacket members movable between an open position in which the
jacket members are separated and a closed position in which
the jacket members are mated together around the inner
jacket and in thermally conductive relation therewith.  The
apparatus also includes a cushion of  thermally conductive,
20   cushioning material disposed inside the inner jacket for
cushioning the bundle when the inner and outer jacket
members are in the closed position.  A window is provided
through the mating inner and outer jacket members for
permitting the passage of light through the window and the
25   tubes of the bundle at  the location of the window.


The present invention also involves a method of cooling
a bundle of capillary tubes to prevent overheating of the
tubes during a parallel capillary electrophoresis procedure.
The method comprises positioning a longitudinal section of
30   the bundle in an open cooling jacket of electrically
insulating, thermally conductive solid material, and
arranging the tubes of the longitudinal bundle section so
that the tubes extend generally parallel and in side-by-side
relation to one another in a generally planar array in the
35   jacket.  The jacket is then closed to enclose within the
jacket said longitudinal section of the bundle from one end

of the section to the other, said tubes of the longitudinal
section being in thermal conductive relation with the
jacket.   The method also includes initiating a capillary
electrophoresis procedure resulting in the generation of
5    heat within the tubes of the bundle, the jacket functioning
to cool said longitudinal section of the bundle to prevent
overheating of the bundle.

Other objects and features will be in part apparent and
in part pointed out hereinafter.

10   Brief Description of the Drawings
Fig. 1 is a schematic view of a capillary
electrophoresis system with cooling apparatus for preventing
overheating of the capillary tubes during a chiral
separation process;
15   Fig. 2 is an enlarged view along lines 2--2 of Fig. 1
showing a conduction cooling device for cooling an array of
closely spaced parallel capillary tubes;
Fig. 3 is an enlarged sectional view of capillary tubes
extending down through power plates into the wells of a
20   microtiter plate;
Fig. 4 is a side elevation of a photodetector mounted
on a rotational stage;
Fig. 5 is a front elevation of a mount for the
rotational stage;
25   Fig. 6 is a front view of an adaptor plate for mounting
the photodetector on the rotational stage;
Fig. 7 is a side view of the adaptor plate;
Fig. 8 is a view of a linear array of photodetector
elements and an image of capillary tubes projected on the
30   array, the linear array being skewed relative to the lengths
of the tubes;
Fig. 9 is a view similar to Fig. 8 but showing the
linear array rotated to a position generally perpendicular
to the lengths of the tubes;
35   Fig. 10 is a front view of certain components of the
cooling device of Fig. 2, including a cooling body;

Fig. 11 is a side elevation of the cooling body of Fig. 10;

Fig. 12 is a side elevation of the cooling body, with the capillary tubes removed;

Fig. 13 is vertical section on line 13--13 of Fig. 10;

Fig. 14 is an enlarged portion of Fig. 13 showing a capillary tube sandwiched between two slabs of the cooling body, a portion of the tube being removed to show details of construction;

Fig. 15 is a front elevation of a back slab of the cooling body;

Fig. 16 is a schematic view of a cleaning and buffer loading system;

Fig. 17 is a schematic view of an alternative CE system using a different cooling apparatus of the present invention;

Fig. 18 is a perspective of the cooling apparatus of Fig. 17;

Fig. 19 is an exploded perspective showing certain components of the apparatus of Fig. 18;

Fig. 20 is a top plan view of the apparatus of Fig. 18;

Fig. 21 is a section on line 21--21 of Fig. 20;

Fig. 22 is an enlarged portion of Fig. 21 showing details of the apparatus and further showing a light source and photo-detector;

Fig. 23 is an enlarged section on line 23--23 of Fig. 20;

Fig. 24 is an enlarged section on line 24--24 of Fig. 20 but showing the various component parts exploded apart.

Corresponding parts are designated by corresponding reference numbers throughout the several views of the drawings.

Detailed Description of the Preferred Embodiment

Referring now to the drawings, Fig. 1 shows a multiplexed (parallel) capillary electrophoresis (CE) system, generally indicated at 1, for separating and

analyzing the components of multiple chemical samples. The system comprises a bundle 3 of capillary tubes 5 having inlet end portions 7 spaced apart (e.g., spread out in a fanned formation) for loading of fluid samples to be

5    analyzed from individual wells 9 (Fig. 3) in a microtiter plate 11 into the tubes, outlet end portions 13 for exit of the fluid samples from the tubes into a waste receptacle 15, and intermediate portions 21 between the inlet and outlet portions arranged in a generally planar, ribbon-like array

10   23 (Fig. 2) in which the intermediate portions extend side-by-side in closely spaced generally parallel relation in a first plane P1. The system also includes a power source 27 for applying a potential (voltage) difference between the inlet end portions 7 and the outlet end portions 13 to cause

15   an electrical current to flow through the contents of the capillary tubes 5, a light source 31 for emitting light to pass through the closely spaced array 23 of intermediate portions 21 of the capillary tubes, and a photodetector generally designated 33 comprising a linear array 34 of

20   photodetector elements (35 in Figs. 8 and 9) in a second plane P2 generally parallel to the first plane P1 for receiving light passing through the planar array of intermediate portions of the capillary tubes. Light passing through the tubes 5 is imaged on the photodetector 33 by an

25   imaging lens, generally designated 39. In accordance with this invention, the system also includes a cooling system, generally indicated at 43, for dissipating the large quantities of heat generated in the capillary tubes 5 and contents thereof during a high-heat separation process, such

30   as a chiral separation process.

More specifically, the capillary bundle 3 may comprise a series of 96 capillary tubes 5, although this number may vary. Each tube 5 is of relatively small diameter (e.g., 50 microns ID; 150 microns OD) and of a suitable electrically

35   nonconductive material, such as fused silica so that high voltages can be applied across tube without generating excessive heat. The tubes 5 may have a polyimide coating

which is removed by a laser beam, for example, in an area
extending across the planar array 23 of intermediate
portions 21 of the capillary tubes, thereby forming what may
be referred to as a detection window (47 in Fig. 2) which is
5   transparent or translucent so that light from the light
source 31 can pass through the walls of the tubes at this
location.  Alternatively, the tubes can be transparent or
translucent along their entire lengths, in which case no
coating removal is necessary.  The bundle 3 is of any
10  appropriate length (e.g., 10 cm- 2 m).  At the detection
window 47 the bundle 3 has a width, designated W in Fig. 2,
in a direction generally perpendicular to its length.  As
illustrated in Fig. 1, the bundle 3 may be supported above
its inlet end portions 7 by a suitable support device 51.
15  The capillary tubes 5 of the bundle 3 may be held in the
aforementioned planar array 23 by any suitable means, such
as by strips of adhesive tape (not shown) extending across
the array on opposite sides of the detection window 47.

        Referring to Fig. 3, the inlet end portions 7 of the
20  capillary tubes 5 extend through tubular sleeves 53 of
electrical insulating material slidably received in holes 55
in a pair of upper and lower metal power plates 57, 59
connected to the power source 27 by suitable electrical
cable 63.  The two plates 57, 59 are secured together by
25  fasteners 65.  The inner end portions 7 of the capillary
tubes 5 extend down beyond the sleeves 53 and into
respective wells 9 in the microtiter plate 11 containing
liquid samples of chemical compositions to be analyzed.
Metal electrodes 69 are secured (e.g., brazed) to the bottom
30  face of the lower power plate 59 and extend down into the
wells 9 alongside the capillary tubes 5 for electrifying the
contents of the wells when the power source 27 is activated.
The power plates 57, 59 and electrodes 69 are preferably of
copper or other suitable metal, and the lower plate 59 and
35  electrodes are preferably gold plated to render them
chemically inert or non-reactive.  To effect chiral
separation, substantially more (3-5 times more) current must

be used than in non-chiral separations. For example, for a bundle of 96 capillary tubes, a total current of 750 milliamps at a voltage of 10,000-30,000 volts may be required to effect separation. A suitable power source for

5   this application is Model 105-30R, available from Bertan High Voltage Corporation located in Hicksville, New York.

The microtiter plate 11 is supported by a thick insulating block 71 of dielectric material which is movable up and down relative to the power plates 57, 59 by a linear

10  actuator generally designated 73. The actuator 73 is operated by rotating a nut 75 relative to a screw shaft 77 in one direction to extend the actuator and thus raise the insulating block 71 and microtiter plate 11, and in the opposite direction to retract the actuator and thus lower

15  the block and microtiter plate. Alternatively, the actuator can be a power (e.g., pneumatic) actuator with suitable controls.

The light source 31 may be of any suitable type, such as a 12-volt deuterium or tungsten lamp or a 254-nm mercury

20  lamp, emitting light having a certain wavelength (e.g., 200-800 nm and generalizable to other wavelengths) corresponding to the absorption band of the sample components of interest. The light is typically ultraviolet or visible light.

The photodetector 33 is of a conventional type, such as

25  a photodiode device, having the aforementioned linear array 34 of photodetector elements 35 (Figs. 8 and 9). These elements may be photodiodes, for example, arranged in one or more linear rows. For example, the photodetector 33 may be a model C5964 multichannel detector head by Hamamatsu

30  incorporating a linear image sensor chip, a low-noise driver/amplifier circuit, and a temperature controller. In this example, the linear image sensor chip has 1024 diodes, each of which is 25 microns in width and 2500 microns height. Other types of photodetectors 33 can be used

35  without departing from the scope of this invention. The photodetector elements 35 generate output signals which are then transmitted to a digital processor 83 (Fig. 1) and

related equipment (e.g., a computer 85) for generating and displaying an electropherogram, i.e., a plot of light intensity versus time, as will be understood by those skilled in this field. This plot can then be evaluated to

5 identify components of interest in the samples being analyzed. As shown in Fig. 1, the electropherogram 87 can be displayed on a screen 89 of the computer 85.

The imaging lens 39 may also be of conventional design, such as a quartz lens (Sodern; f.1.= 94mm; F=4.1) in

10 combination with an interference filter 93 (Oriel) employed to define the absorption wavelength. The lens 39 is positioned between the detection window 47 and the photodetector 33 to receive light passing through the capillary tubes 5 and to image that light on the linear

15 array 33 of photodetector elements 35. The image of the capillary tubes 5 projected by the lens 39 on the photodetector 33 may be an image 1.5 times actual size, for example.

Referring to Figs. 1 and 4, a mounting assembly,

20 generally designated 99, is provided for mounting the photodetector 33 for rotation about a generally horizontal axis A. This assembly 99 comprises a bracket 101 attached to the floor 103 of an enclosure to be described later in detail, a vertical mounting plate 107 attached to the

25 bracket and extending up from the bracket, and a rotational stage, generally designated 109, attached to the mounting plate. The rotational stage 109 comprises a stationary ring unit 113 attached to the mounting plate 107, and a rotatable ring unit 115 concentric with the stationary ring unit and

30 rotatable relative thereto about the aforesaid horizontal axis A. The rotational stage 109 has a gross angular adjustment (e.g., a set screw arrangement not shown) whereby the rotatable ring unit 115 can be quickly rotated to an approximate angular position, and a fine angular adjustment

35 (e.g., a screw-type adjustment 121) whereby the angular position of the rotatable ring unit can be slowly moved to a precise position, the angular adjustment mechanism then

functioning to hold or maintain the ring unit in such
precise position until such time as further adjustment is
required.  Alternatively, a locking mechanism separate from
the angular adjustment mechanism may be used to maintain the
5  rotatable ring unit in its adjusted position.  The vertical
mounting plate 107 has a central opening 125 therein aligned
with the openings in the ring units 113, 115.  The type of
rotational stage 109 shown in the drawings is generally of a
type which is commercially available, e.g., Model UTR Series
10  Manual Rotary Stage sold by Newport Corporation of Irvine,
California.

Referring to Figs. 4, 6 and 7, means generally
indicated at 125 is provided for attaching the photodetector
33 to the rotatable ring unit 115 of the rotational stage
15  109.  This means comprises an adaptor, also designated 125,
comprising a frame 127 of suitable material (e.g., anodized
aluminum) defining an opening 129, fasteners 131 (e.g.,
screws) receivable in fastener openings 133 in the frame for
fastening the adaptor to the front face of the photodetector
20  33 with the opening 129 in the frame aligned with the linear
array 34 of photodetector elements 35, and fasteners 135
(e.g., screws) receivable in fastener openings 137 in the
frame for fastening the adaptor to the rear face of the
rotatable ring unit 115 of the rotational stage 109 with the
25  frame opening 129 aligned with the opening in the ring unit
115, the openings in the two ring units 113, 115 and the
adaptor 125 being sufficiently large to expose the entire
linear array 34 of the photodetector 33 to light transmitted
by the lens 39.  When the photodetector 33 is attached to
30  the rotatable ring unit 115, the unit can be rotated on axis
A to adjust the angular orientation of the linear array 34
of photodetector elements 35 relative to the image of the
capillary tubes 5 projected by the lens 39 onto the
photodetector.  Suitable markings (not shown) are provided
35  on the ring units 113, 115 for reading the angular
orientation of the rotatable ring unit 115 relative to the
stationary ring unit 113.  The markings should be

sufficiently close together to measure very small increments
of rotation (e.g., 1/60 of one degree) to provide very fine
adjustment.

5    Other types of rotational stages and/or mounting
assemblies for the photodetector 33 may be used without
departing from the scope of this invention. Also, the
rotatable ring unit 115 of the rotational stage 109 may be
rotatable manually or by a suitable motorized mechanism.

Referring now to Fig. 1, the cooling system 43 of the
10   present invention comprises a thermally insulated enclosure
145 enclosing the bundle 3 of capillary tubes 5, light
source 31 and photodetector 33. The cooling system includes
a first heat transfer mechanism comprising a conduction heat
transfer mechanism, generally designated 151, for cooling
15   the array 23 of closely spaced intermediate portions 21 of
the capillary tubes, where the density of the tubes
generates a substantial amount of concentrated heat, and a
second heat transfer mechanism comprising a pair of
convective heat transfer units, each generally indicated at
20   155, for cooling the inlet end portions 7 of the tubes 5
which, unlike the intermediate portions 21, are spread apart
and not closely packed.

The enclosure 145 can be in the shape of a large box,
having front doors 161 for access to the interior of the
25   enclosure. The enclosure is provided with a layer of
thermal insulation 163.

In the preferred embodiment shown in Figs. 2 and 10-15,
the conduction heat transfer mechanism 151 comprises a
refrigerated body 165 of thermally conductive material
30   (e.g., a metal such as aluminum) having a length L1 and a
width W1. The body is supported in the enclosure 145 by a
post P and comprises two separate rectangular slabs, i.e., a
relatively thick front cooling slab 167 having a front face
169 and a rear face 171, and a thinner back slab 173 having
35   a front face 175 and a rear face 177. The slabs have
central aligned window openings 181 therein which combine to
form a window, also designated 181, through the body.

Referring to Fig. 15, the window 181 has a width W2 greater than the width W  of the bundle 3 and a length L2 sufficient to expose the bundle for testing, in this case to permit the passage of light from the light source 31 through

5    the window 181 for incidence on the aforementioned detection window 47 of the capillary bundle 3.

The front slab 167 has passaging therein for the flow of a suitable coolant to cool the slab.  (The coolant may be water or other liquid.)  This passaging comprises a pair of

10   passages constituted by bores 185, 187 through the slab 167 located on opposite sides of the window 181.  The bores 185, 187 are sealingly connected by flexible tubing, as indicated at 191.  Bore 187 has an inlet end for connection to a coolant supply line 195 of a suitable refrigeration system

15   197, and bore 185 has an outlet end for connection to a coolant return line 201 of the same refrigeration system. The refrigeration system 197 may be conventional, such as a Model RTE Series refrigerated bath and recirculating system commercially available from NESLAB Instruments, Inc. of

20   Portsmouth, NH.  This system has a temperature control, including a temperature sensor (not shown) for sensing the temperature of the cooling body 165, so that the temperature of the body can be regulated.

As illustrated best in Fig. 15, the back slab 173 has a

25   channel 205 in its front face 175 which extends the full length L1 of the slab about midway between opposite sides of the slab (the top and bottom sides as shown).  When the back slab 173 is attached to the front slab 167, as by fasteners 207, the rear face 171 of the front slab 167 and the walls

30   of the channel 205 combine to define a recess 211 (Fig. 14) which is generally rectangular in horizontal section for receiving the bundle 3 of capillary tubes 5.  This recess 211 has a width W3 (Fig. 15) slightly greater than the width W of the bundle 3 at the detection window 47, and a depth

35   (front-to-back direction) which is approximately equal to the diameter of a capillary tube 5 of the bundle, so that the tube is positioned sufficiently close to the rear

cooling face 171 of the front slab 167 for the efficient
transfer of heat from the tube (and its contents) to the
body 165.   Preferably, the bundle 3 is in contact with the
cooling face 171, but actual contact is not essential so

5   long as sufficient cooling is provided.   The recess 211 is
positioned relative to the window 181 so that when the
bundle 3 is in position, the bundle is aligned with the
window so that light transmitted through the window will
pass through the capillaries.

10     The front and back slabs 167, 173 are electrically
insulated from the capillary tubes 5 by coatings 215 of a
suitable dielectric material (e.g., alumina from an
anodizing process) applied at least to the rear face 171 of
the front slab 167 and the front face 175 of the back slab

15   173 (Fig. 14).   The coating 215 should be thermally
conductive and may have a thickness of 0.5-2.0 $\mu$m, for
example.

     The fasteners 207 for connecting the two slabs 167,
173, are illustrated in Fig. 11 as bolts received in holes

20   adjacent the four corners of the slabs, the holes in the
front slab 167 being non-threaded clearance holes which are
counterbored to receive the heads of the bolts, and the
holes in the back slab 173 being tapped.   Other fastening
arrangements may be used.

25     The slabs 167, 173 may be dimensioned according to the
required cooling requirements.   Preferably, the slabs have a
length L1 sufficient to cover a substantial portion of the
length of the bundle 3 to provide the desired cooling.   The
slabs 167, 173 should also have a sufficient mass and

30   thermal conductivity to be quickly responsive to temperature
adjustments which may be  made, as by the aforementioned
temperature control of refrigeration system 197.

     Other heat transfer mechanisms may be used for cooling
the closely spaced array of capillary tubes 5.   For example,

35   a thermoelectric device can also be used.

     Each convective heat transfer unit 155 comprises a heat
exchange device 221 having a cooling surface and a fan 225

for circulating air over the cooling surface and directing
such air in an appropriate direction.  One of the two units
155 is preferably located adjacent the inlet end portions 7
of the capillary tubes 5 for circulating cool air thereover;
5   the other is preferably located adjacent the photodetector
33, as illustrated in Fig. 1.  The two heat exchange devices
221 are operable to maintain the air temperature inside the
enclosure in the range of 0-90 degrees C., and preferably at
about 10 degrees C.  Suitable convective heat transfer units
10  of the type described are available, one such unit being
available under the trade designation Kodiak Recirculating
Chiller - RC022J02BG3 from Lytron Inc. of Woburn, MA.  Other
devices may also be used for circulating cooling air inside
the enclosure 145 without departing from the scope of this
15  invention.

       Figs. 1 and 16 illustrate a system generally designated
231, for flushing the capillary tubes 5 and also for loading
the tubes with a suitable buffer solution prior to
conducting an actual sample separation process.  The system
20  231  includes a pump 233 having an inlet 235 for selective
connection via a line 236 to a first container 237
containing a supply of flushing solution (e.g., water or an
aqueous solution of sodium hydroxide) or to a second
container 241 containing a supply of buffer solution (e.g.,
25  cyclodextrin for chiral separation).  The pump 233 has an
outlet 243 connected via line 245 to a manifold 247 having a
series of outlet ports 249.  Each outlet port 249 is
connected to a conduit 251 which extends to one end of a
fitting 253 mounted on a support 255 in the enclosure 145,
30  the other end of the fitting being connected to a group 5a
of capillary tubes.  (For example, a capillary bundle
consisting of 96 capillary tubes may be divided into eight
groups 5a of 12 tubes each, and each group may be connected
to a respective fitting 253.)  The arrangement is such that
35  the pump 233 may be operated to pump liquid from the
appropriate container 237, 241 for delivery to the capillary
tubes 5 via line 245, manifold 247, conduits 251 and

fittings 253.  The fittings are of conventional design and
commercially available, e.g., from Valco Instruments
Company, Inc. of Houston, TX.

In use, the CE system 1 of the present invention is set
5   up as shown in Fig. 1, where the array 23 of the
intermediate portions 21 of the parallel capillary tubes 5
lie in a first plane P1 within the channel 205 of the
cooling body 165, where the photodetector 33 is mounted on
the rotational mount 109 in a position in which the linear
10  array 34 of photodetector elements 35 lies in a second plane
P2 generally parallel to the first plane P1, and where the
axis of rotation A is generally perpendicular to the two
planes P1, P2.  (As used herein, "generally parallel"
includes an arrangement where the two planes P1, P2 are off
15  parallel by as much as 5 degrees.  Similarly, "generally
perpendicular" includes an arrangement where the axis A is
off perpendicular by as much as 5 degrees.)

The capillary tubes 5 are cleaned ("conditioned") and
prepared prior to the start of each sample separation run.
20  This is accomplished by connecting the outlet end portions
13 of groups 5a of the capillary tubes 5 to respective
fittings 253 on the support 255, and then operating the pump
233 to pump cleaning solution from the cleaning solution
receptacle 237 through the capillary tubes, the flow being
25  in a direction toward the inlet end portions 7 of the tubes.
A microtiter plate 11 is positioned on the insulating block
71 to receive cleaning solution as it exits the tubes.
After the capillary tubes 5 have been flushed (e.g.,
"conditioned"), the inlet 235 of the pump 233 is connected
30  to the container 241 containing buffer solution, and the
pump is then operated to fill the capillary tubes with
buffer solution.  After the capillary tubes are properly
cleaned and prepared, samples are loaded into the tubes.
Sample loading is accomplished by disconnecting the outlet
35  end portions 13 of the capillary tubes from their respective
fittings 253 and placing the outlet end portions in the
waste receptacle 15.  A microtiter plate 11 containing the

samples to be analyzed is positioned on the insulating block 71 with the capillary tubes 5 and electrodes 69 extending down into the wells 9 of the plate.  The power source is then operated to apply a voltage differential (e.g., 10 kv)

5   across each capillary tube for a period of time (e.g., 10 seconds) suitable to cause the electro-kinetic movement of a quantity of sample from the wells 9 of the microtiter plate 11 into the inlet end portions 7 of the capillary tubes. After samples have been loaded into the capillary tubes, the

10  microtiter plate 11 is replaced by a container of buffer solution so that the inlet end portions 7 of the capillary tubes extend down into the buffer solution.  The buffer solution container may be wrapped or otherwise sealed to reduce evaporation of the buffer.

15      Following sample loading, and prior to the start of an electrophoresis operation, the cooling system 43 is actuated to cool the interior of the enclosure 145 and the capillary tubes 5 therein.   This involves actuating the two convective cooling units 155 and also the conduction cooling

20  device 151 for a time sufficient to bring the interior air temperature of the enclosure 145 down to a temperature sufficient to prevent overheating of the capillary tubes and the contents thereof during chiral separation.  A temperature in the range of 0-90 °C, and preferably about 10°

25  C or lower, is believed to be suitable for this purpose.

        After the enclosure 145 and capillary tubes 5 are suitably cooled, a voltage is applied to the tubes, causing the various components of the samples to migrate at different speeds to effect separation, as will be understood

30  by those skilled in this field.  To separate chiral molecules, usually a relatively large current is required (e.g., a sum total of 20 milliamps for a bundle of 96 capillary tubes), which results in the generation of a substantial amount of heat in the tubes and contents

35  thereof.  The conduction heat transfer device 151 removes this heat in the area of the bundle 3 generally adjacent the detection window 47, where the capillary tubes 5 are

relatively closely spaced.  The convective heat transfer
units 155 removes this heat from other portions of the
bundle, including the inlet end portions 7 of the tubes 5.
As a result, overheating of the capillary tubes and contents
5    thereof is prevented, thus ensuring a more accurate analysis
of the samples.

Light from the light source 31 passes through the
planar array 23 of the capillary tubes and is projected by
the lens 39 as an image of the tubes onto the photodiodes 35
10   of the photodetector 33.  These diodes 35 generate signals
which are processed in conventional fashion to generate and
display an electropherogram 87 plotting light intensity
(indicative of absorption levels) versus time.  The clarity,
resolution and detection limits of this plot can be improved
15   by rotatably adjusting the rotatable ring unit 115 (carrying
the photodetector 33) to find the optimal angular position
for providing an electropherogram having better clarity,
resolution and/or detection limits.  The adjustment
procedure is best illustrated in Figs. 8 and 9.

20       In Fig. 8, it will be observed that the image of the
tubes 5 projected on the linear array 34 of photodiodes is
at an angle where the longitudinal centerline 275 of the
array is skewed at an angle B relative to the centerline 277
of a tube 5.  This orientation does not yield an optimal
25   electropherogram, since the photodiode elements 35 are
slanted relative to the lengths of the tubes.   The
characteristics (clarity, resolution and/or detection
limits) of the electropherogram can be improved by rotating
the rotatable ring unit 115 of the rotational stage 109, and
30   the photodetector 33 mounted thereon, to the position shown
in Fig. 9 where the photodiode elements 35 are more aligned
with the projected image of the tubes 5.  The optimal angle,
indicated at C in Fig. 9, is usually about 90 degrees, that
is, an angle where the longitudinal centerline 275 of the
35   linear array 34 of photodetector elements 35 is precisely
perpendicular to the capillary tubes (i.e., the projected
image of the tubes) and the longitudinal centerlines of the

elements 35 are parallel to the longitudinal centerlines 277
of the capillary tubes.  The optimal angle is identified by
rotating the rotatable ring unit 115 one way or the other
until the display of the electropherogram 87, as it appears
5   on the screen 89, is optimal in terms of clarity, resolution
and/or detection limits.  The ring unit 115 is then
maintained in this position throughout the separation
process.  The precise position of the rotatable ring unit
115 relative to the stationary ring 113 unit can be recorded
10   by using the markings on the two units.

It will be understood from the foregoing that the
system described above optimizes the results of a parallel
CE operation by improving the clarity, resolution and/or
detection limits of electropherograms generated during the
15   separation and analysis process.  This is achieved by a
method involving rotating the photodetector 33 relative to
the projected image of the capillary tubes to a position in
which the array 34 of photodetector elements 35 is at an
optimal orientation (e.g., as shown in Fig. 9), relative to
20   the image, and then maintaining the photodetector in such
position.  The optimal orientation is easily determined
simply by watching the electropherogram while rotating the
photodetector 33 until the display of the electropherogram
is optimal.

25      It will also be observed that the cooling system 43 of
this invention will provide efficient well-regulated cooling
of the bundle 3 by using the convective and conductive heat
transfer devices 151, 155, the conductive device providing
additional cooling of the tubes 5 where they are more
30   closely spaced in the area adjacent the window 181 in the
body 165 where the samples in the tubes 5 are exposed for CE
analysis.  Consequently, even during chiral separation and
other CE processes generating large amounts of heat, the
temperature of the samples will remain well below boiling to
35   avoid the formation of bubbles in the samples which can
cause dielectric breakdown, sparking and other undesirable
results adversely affecting sample analysis.  The system of

the present invention can be used for any parallel or
multiplexed CE process, including but not limited to the
separation of chiral molecules.  It is believed that the
system described above is the first parallel CE system
5   designed to effect chiral separation.

Chiral separation using parallel CE can be effected
with or without the use of circular dichroism ("CD") which
is the differential light absorption properties of left and
right circularly polarized light and which is a
10   characteristic spectroscopic property of chiral molecules.
When CD is used, the throughput can be greatly improved
because the separation of enantiomers is not required
resulting in a shorter separation/detection times.  CD can
be used to quantitatively identify enantiomeric excess in
15   the presence of both enantiomers of a chiral species.  The
system described above can be modified to use CD by placing
a photoelastic modulator between the light source 31 and the
detection window 47 of the capillary tubes.  The modulator
modulates the light between the left and right circularly
20   polarized components.  The magnitude of the CD signal is
determined by taking the difference between the left and
right hand signals at the photodetector 33.  CD is commonly
determined for absorption but can also be determined from a
fluorescence signal in a fluorescence detection (rather than
25   light absorption) system.  In such a system, an analyte
which emits upon illumination (either naturally or via a
chemical tag) can be used.  In this case, an intense source,
lamp or laser, illuminates the capillary array and the
resulting emission is detected by the diode array.
30   While the cooling system of the present system is an
important aspect of the present invention, it is
contemplated that cooling of the bundle 3 during parallel CE
may not be necessary under all circumstances, in which case
the cooling devices 151, 155 and/or enclosure 145 may be
35   eliminated.

Fig. 17 shows another embodiment of a parallel CE
system, generally designated 281.  The system includes

different cooling apparatus comprising a solid-state cooling
device, generally designated 283, for cooling a bundle B of
capillary tubes.  The system also includes a pair of
hydrodynamic injectors 285, 287 at opposite ends of the
5    bundle for conditioning and filling the tubes of the bundle.
One of the injectors (285) is grounded and the other (287)
is connected to a suitable power source 289 similar to the
power source 27 of system 1.  The construction and operation
of these injectors 285, 287 are described in detail in
10   pending application Ser. No. 9/620,987, filed July 21, 2000,
by Peijun Cong et al., entitled Hydrodynamic Injector,
assigned to Symyx Technologies, Inc., and incorporated by
reference herein.  The injectors eliminate the need for the
pump 233, manifold 247, fittings 253 and support 255, among
15   other things, of the system 1 of the first embodiment.  As a
result, there is no need to make the many fitting
connections and disconnections during conditioning and
filling, thereby reducing the risk of damage to the
capillaries.  A number of fans 291 are provided for blowing
20   cooling air on the injectors 285, 287 and the cooling device
283 to be described.  Like system 1 describe above, the
system 281 of this embodiment includes a light source 293
(e.g., deuterium lamp) for emitting light to pass through
the capillary tubes in a manner to be described, a bandpass
25   filter 295, a lens 297 and a photodiode array detector 299
connected to a suitable digital processor and related
equipment 301.

    Figs. 18-24 show details regarding the construction of
cooling device 283.  This device is designed to contact a
30   bundle B of capillary tubes over a major portion of its
overall length, and preferably over as much of the bundle
length as possible, to provide adequate cooling during a CE
procedure generating substantial heat.  In most cases the
cooling device will extend over at least 50% of the overall
35   length of the bundle, and preferably over at least two-
thirds of the overall bundle length.

In the particular embodiment shown in Figs. 18-24, the
solid-state cooling device comprises inner and outer jackets
designated 305 and 307, respectively.  The device also
includes a cushion, generally indicated at 309 in Fig. 24,
5   inside the inner jacket for protecting against damage to the
capillary tubes placed inside the jackets.  These components
are described in more detail below.

The inner jacket 305 of the particular embodiment shown
in the drawings comprises opposing elongate inner jacket
10  members in the form of channel-shaped slabs 313.  The slabs
have opposing webs 315 and flanges 317 which combine to
define recesses for receiving the aforementioned cushion
therein 309.  (The precise shape of the inner jacket members
313 is not critical, and configurations other than those
15  depicted in the drawings are contemplated.)  The inner
jacket members 313 are movable between an open position
(Figs. 18, 23) in which the members are separated to allow
placement of the bundle in the jacket, and a closed position
(Fig. 22) in which the jacket members are mated together in
20  a position in which they surround the capillary tubes of the
section of the bundle B placed in the jacket.  The inner
jacket 313 members are of a solid, thermally conductive,
electrically insulating material.  This material is
preferably a ceramic-like material having excellent thermal
25  conductivity and dielectric strength characteristics.  One
such material is boron nitride, which is particularly
desirable because it is capable of being machined and is
also relatively inexpensive, but other materials (e.g.,
silicon nitride) may also be suitable.  The material used
30  preferably has a thermal conductivity in the range of about
5-50 W/m-K, and more preferably in the range of about 15-50
W/m-K, and dielectric strength in the range of about 20-400
kV/mm, and more preferably in the range of about 40-200
kV/mm.  These properties are important to insure proper
35  cooling when high levels of power are applied to the bundle
during certain CE procedures.  By way of example, when CE is
run in the micellar electrokinetic chromatography (MEKC)

mode, the amount of power applied to the bundle may range
from 150-200 watts, with voltages ranging from 10,000-30,000
volts.  The use of this amount of power results in the
generation of substantial temperature rises inside the
5   capillary tubes due to Joule heating, and good thermal
conductivity is essential to provide adequate heat transfer
away from the tubes for adequate cooling.  Without such heat
transfer, capillary temperatures could rise to levels where
the procedure is adversely affected, or where there is a
10  complete failure of the system.  Further, high voltages can
create static electrical charges on the outside surfaces of
the capillary tubes.  Accordingly, good electrical
insulation properties are necessary to prevent an electrical
connection between the ends of the tube through the cooling
15  apparatus.  Also, high dielectric strength is necessary to
prevent shorting between the capillary and the outer jacket
307, the latter of which typically is of metal, as will be
described later.
        The cushion 309 is of a thermally conductive,
20  cushioning material.  In one preferred embodiment, the
cushion comprises a pair of opposing sheets 321 disposed
between the inner jacket members 313 on opposite sides of
the bundle B and extending the full length of the inner
jacket 313.  The cushion sheets 321 are preferably of a
25  conformable material, and more preferably an elastomeric
material  (e.g., a silicone-based elastomer, such as is
available from Thermagon, Inc. of Cleveland, Ohio
(www.thermagon.com) under the trade designation T-pli 230),
although other materials having the requisite thermal
30  conductivity and cushioning characteristics may also be
used.  In this regard, the thermal conductivity of the
cushion sheet material is preferably in the range of about
3-9 W/m-K, and more preferably in the range of about 5-7
W/m-K.  The sheet material may also be electrically
35  insulating, although this is not critical.  In the
embodiment shown in the drawings, the sheets 321 nest within
the recesses defined by the webs 315 and flanges 317 of the

slabs forming the inner jacket members 313.  The cushion
sheets 321 are preferably in good thermal contact with at
least the webs of the inner jacket members.  A suitable
thermal grease (e.g., a silicon based zinc oxide grease) can

5    be used between the sheets 321 and inner jacket members 313
to enhance thermal conductivity, if desired.  Suitable
thermal grease is available from Materials Electronic
Products Corporation of Trenton, New Jersey
(www.melcor.com), under the trade designation TG-001, having

10   a thermal conductivity of about 0.735 W/m-K.

The outer jacket 307 surrounds the inner jacket 305 and
may comprise, in one embodiment, mating elongate outer
jacket members 331.  The outer jacket members 331 are of a
thermally conductive material, preferably metal (e.g.,

15   aluminum).  Each outer jacket member 331 is of generally
channel shape, having a base 333 and a pair of spaced side
walls 335 extending out from the base.  Other configurations
are possible.  The outer jacket members 331 are movable
between an open position (Figs. 19, 24) in which the parts

20   are separated, and a closed position (Figs. 18, 21, 23) in
which the jacket members are mated together in a position
surrounding the inner jacket 305.  When the outer jacket 307
is closed, the inner jacket members 313 are received in the
recesses formed by the channel shaped outer jacket members,

25   with the webs 315 of the inner jacket members 313 being
disposed in thermal conductive relation with the bases 333
of the outer jacket members 331 and with the ends of the
flanges 317 of each inner jacket member being generally
flush (coplanar) with the free ends of the side walls 335 of

30   a respective outer jacket member 331.  A layer of the
aforementioned thermal grease may be applied between at
least the webs 315 of the inner jacket members 313 and the
bases 333 of the outer jacket members 331 to enhance thermal
conductivity, if desired.  The overall width of each inner

35   jacket member 313 is slightly less than the distance between
the side walls 335 of the corresponding outer jacket member
331, so that the fit of the inner jacket member between the

side walls of the outer jacket member is relatively close.
(Actual contact of the inner jacket members 313 with the
side walls 335 of the outer jacket members 331 is not
necessary, because the primary path of heat transfer is
5    though the webs and bases of the jacket members.)  The
distance between the flanges 317 of each inner jacket member
313 will vary depending on the number of capillary tubes in
the bundle B, which typically includes 24, 48 or 96 tubes
but which may include any number of tubes.  In any event,
10   the distance between the flanges 317 should be somewhat
greater than the combined diameters of the tubes of the
bundle to provide sufficient space to arrange the tubes in
an even, side-by-side planar array without undesirable
bunching of the tubes which could detrimentally affect the
15   results of the CE procedure.

The inner and outer jackets 305, 307 are secured
together by suitable means, such as threaded fasteners (not
shown) passing through bores 341 in the side walls 335 of
the outer jacket members 331.  In one embodiment, tightening
20   of these fasteners functions to draw the inner and outer
jacket members 305, 307 closer together, causing the cushion
sheets 321 to press against opposite sides of the array of
capillary tubes in the apparatus.  A small compressive force
is desirable (although not essential) for increasing thermal
25   conductivity between the capillary tubes and the cushion
sheets 321.  The resultant pressure may also assist in
enhancing the thermal conductivity between the cushion
sheets 321 and the inner jacket members 313, and between the
inner jacket members 313 and the outer jacket members 331.

30       The inner and outer jacket members 313, 331 are formed
with window openings 351, 353, respectively (Fig. 22).
Similarly, the cushion sheets are formed with window
openings 355.  When the jackets 305, 307 are closed, these
window openings 351, 353, 355 align with one another to
35   define a window, generally designated 357, for permitting
the passage of light through the window and the capillary
tubes of the bundle B at the location of the window.  As

shown in Fig. 21, the window 357 exposes a portion of a bundle B of capillary tubes contained within the apparatus to light emanating from the light source 293, which may be similar to the light source 31 described earlier in this

5      specification.  Light incident on the bundle B creates an image of the bundle which may be projected on the photo-detector 299 (Fig. 21) or other piece of equipment used to analyze the contents of chemical samples passing through the tubes.  If a photo-detector is used, it may be similar to

10     the device 33 described previously in this specification. The dimensions of the window 357 are not critical, except to say that the window is preferably relatively narrow lengthwise of the bundle (e.g., 2 mm.)

       The outer jacket members may be equipped with one or

15     more heat sinks, each generally designated 361, for increasing the heat absorption and dissipating capacity of the apparatus.  In the particular embodiment shown in the drawings, the heat sinks may comprise one or more banks of parallel cooling fins or plates 363 mounted (e.g., fastened)

20     on the base of each of the upper and lower outer jacket members 331.  The heat sink 361 may be of any suitable conventional construction, such as a bonded fin heat sink commercially available from, e.g., Materials Materials Electronic Products Corporation of Trenton, New Jersey

25     (www.melcor.com),part number HX8-202. Fan forced convection may be used to provide additional cooling, if needed.

       As illustrated, the inner and outer jackets 305, 307 are elongate and of approximately the same length.  This length is preferably sufficient for enclosing a major

30     portion of the length of the bundle B.  For example, the jackets may be dimensioned to enclose at least about 50% of the overall length of the bundle, and more preferably about two-thirds of the overall length.  (The length of a typical bundle will range from about 20-60 in.)  For ease of

35     assembly, and because the inner jacket members 313 may be of a material (e.g., boron nitride) which is available only in certain standard lengths, it may be desirable or even

necessary to manufacture the inner and outer jacket members 313, 331 in multiple pieces.  In the embodiment shown in the drawings, each inner jacket member 313 is formed in four pieces, as is the upper outer jacket member 331.  The lower

5   outer jacket member 331 is formed as a single piece.  As will be described later, the jacket pieces are assembled end-to-end to make jacket members 313, 331 of the appropriate length.

The cooling apparatus 383 may be mounted in the

10   generally horizontal position shown in Fig. 17 with one outer jacket member 331 disposed above the other outer jacket member 331.  In this embodiment, the lower outer jacket member 331 is held by a plurality of brackets 371 supported by posts 373.  The posts are preferably of an

15   electrically insulating material (e.g., Delrin®) to electrically isolate the outer jacket 307 from its surroundings.   It will be understood that the cooling apparatus could be mounted in other orientations and using other types of supports.

20   To use the cooling apparatus shown in Figs. 17-24, the inner and outer jackets 305, 307 are disassembled to expose the lower outer jacket member 331 so that a thin layer of thermal grease may be applied to the upper surface of the base 331 of the jacket member.  The lower inner jacket

25   member 313 is then placed between the side walls 335 of the outer jacket member 331 and slidably moved (rubbed) back and forth along the base 333 until good thermal contact between the web 315 of the inner jacket member and the base 333 of the outer jacket member is established and the window

30   openings 351, 353 in the two lower jacket members 313, 331 are in alignment.  The lower cushion sheet 321 is placed over the web 315 of the inner jacket member 313 and a window opening 355 is cut in the cushion sheet in alignment with the window openings in the jacket members therebelow.   The

35   window opening 355 could also be pre-cut in the cushion sheet 321.  Alternatively, the cushion sheet could be divided into two longitudinal sections spaced apart to

define a window opening.  In any event, a layer of thermal
grease can be applied, if desired, between the lower cushion
sheet 321 and the web 315 of the lower inner jacket member
313.  After the lower cushion sheet is in place, a section
5     of the capillary bundle B is placed on the lower cushion
sheet 321 in an arrangement wherein the capillary tubes are
in a planar parallel array extending the length of the
jacket members 313, 331 and side-by-side between the flanges
317 of the lower inner jacket member 313.  As so positioned,
10    the tubes are preferably evenly spaced and close together,
if not in actual contact, out of contact with the flanges of
the lower inner jacket member.

After the capillary tubes have been suitably arranged,
the upper cushion sheet 321 and upper jacket components 313,
15    331 are assembled in similar fashion.  That is, the upper
cushion sheet 321 is placed on top of the bundle and a
window opening 355 is cut (or pre-cut) in alignment with the
lower window openings 351, 353.  Alternatively, the cushion
sheet 321 could be divided into two longitudinal sections
20    spaced apart to define a window opening.  The upper inner
and upper outer jacket members 313, 331 are then placed in
position, with the window openings 351, 353 aligned and the
entire assembly secured by fasteners.  If the upper inner
and outer jacket members are each formed in multiple pieces,
25    as shown in Fig. 19, the relatively short window piece of
the inner jacket member 313 is preferably placed in position
first, thus ensuring that the window opening 351 in this
piece is properly aligned with the window openings below it,
and that the tubes of the bundle are in the desired final
30    position.  Once this window piece is positioned, the other
pieces of the inner jacket member 313 can be assembled end
to end.  The same procedure is followed using the pieces of
the upper outer jacket member 331.  Again, thermal grease
may be used where appropriate.
35    The upper and lower jacket members 305 307 are secured
together by suitable means, such as the threaded fasteners.
The components of the jacket are sized and configured

relative to one another so that when the jackets are secured
in their closed position, the bundle B, cushion sheets 321,
and inner and outer jackets 305, 309 are in close thermal
contact with one another and, preferably, the bundle is

5   subjected to a light compressive force to further enhance
thermal conductivity for the efficient transfer of heat
generated during a CE procedure from capillary tubes out
through the cushion sheets and the jacket members for
suitable dissipation.  As noted above, this dissipation may

10  be increased by the use of optional heat sinks 361.  Besides
providing excellent thermal conductivity, the inner jacket
305 functions to electrically insulate the bundle from the
outer metal jacket 307.  The cushion sheets 321 function to
cushion the capillary tubes to prevent damage thereto when

15  the jackets are secured in closed position.

        After the jackets 305, 307 are secured in their closed
positions, a CE procedure using high-voltages may be
initiated in a conventional manner.  The solid-state
cooling apparatus of the present invention effectively cools

20  the bundle B over a substantial length of the bundle while
also electrically insulating the bundle to prevent the flow
of current on the outside of the tubes.  Further, since the
tubes of the bundle are located inside the jackets, they are
protected against damage and remain well organized.

25      It will be understood that the embodiments described
above are intended to be illustrative only, and other
embodiments are contemplated as falling within the scope of
this invention.  For example, it is contemplated that a
solid-state cooling device of the present invention could

30  comprise only a single jacket corresponding to the inner
jacket 305 described above.  In other words, the outer
jacket 331 could be eliminated altogether.  Further, the
cushion 309 for protecting the capillary tubes could take
many forms, and could even be eliminated entirely.  Also,

35  while the inner jacket members 313 and outer jacket members
331 are illustrated as being symmetric, non-symmetric parts
can be used.

The specific dimensions of the jacket components will
vary depending on the particular application, but generally
speaking, the lengths of the inner jacket 305 and outer
jacket 307 are preferably such as to enclose a major portion
5    of the length of the bundle, and preferably as much of the
length of the bundle as possible.  Further, the thicknesses
of the base 333 of each outer jacket member 331, the web 315
of each inner jacket member 313 and a cushion sheet 321
should be sufficient to achieve the objectives set forth
10   above.  In general, the temperature differential between the
center of each capillary tube and the outer surfaces of the
outer jacket members 331 should be no greater than about 10
degrees K, and the various material thicknesses and thermal
conductivities should be selected accordingly.  In one
15   embodiment, for example, each outer jacket member 331 is of
aluminum having a thermal conductivity of about 237 W/m-K
and a base thickness of about 5 mm.; each inner jacket
member 313 is of boron nitride having a thermal conductivity
of about 15-50 W/m-K and a web thickness of about 5 mm.; and
20   each cushion sheet 321 is of a silicone elastomer having a
thermal conductivity of about 6 W/m-K and a thickness of
about 0.3mm.  A typical capillary tube has an OD of about
150-375 microns and a thermal conductivity of about 1.5 W/m-
K, a larger diameter tube being less fragile than a smaller
25   diameter tube.  It will be understood, therefore, that
different combinations of materials and thicknesses can be
used to stay within the preferred maximum temperature
differential of 10 K.

    To reduce the aforementioned temperature differential,
30   the thickness of the jacket members 313, 331 can be reduced.
However, the lower thickness limits for certain materials
may be limited by their dielectric breakdown voltage.  For
boron nitride, for example, this value is 40-200 kV/mm.
Thus, to provide proper electrical insulation at a voltage
35   of 30 kV, a minimum thickness of 0.75 mm of BN is needed.
As a practical matter, the lower limit of thickness may be
determined by the fragility of the material.  To replace BN

with a different material, that material should possess the appropriate thermal conductivity and electrical insulation properties. As noted previously, one such material is aluminum nitride having a thermal conductivity of 100 W/m-K

5   and a dielectric strength of 40 kV/mm. However, this material is significantly more expensive and harder to machine.

When introducing elements of the present invention or the preferred embodiment(s) thereof, the articles "a", "an",

10  "the" and "said" are intended to mean that there are one or more of the elements. The terms "comprising", "including" and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements.

15  In view of the above, it will be seen that the several objects of the invention are achieved and other advantageous results attained.

As various changes could be made in the above constructions without departing from the scope of the

20  invention, it is intended that all matter contained in the above description or shown in the accompanying drawings shall be interpreted as illustrative and not in a limiting sense.